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Evidence Report/Technology Assessment
Number 93

Effects of Omega-3 Fatty Acids on Cardiovascular Risk Factors and Intermediate Markers of Cardiovascular Disease

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-Based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. This report on Effects of Omega-3 Fatty Acids on Cardiovascular Risk Factors and Intermediate Markers of Cardiovascular Disease was requested and funded by the Office of Dietary Supplements, National Institutes of Health. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review prior to their release.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

We welcome written comments on this evidence report. They may be sent to: Director, Center for Outcomes and Evidence, Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850.

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The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services of a particular drug, device, test, treatment, or other clinical service.

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Structured Abstract

Context. Epidemiologic studies and clinical trials have reported beneficial effects of fish/omega-3 fatty acid consumption on several cardiovascular disease (CVD) outcomes, such as sudden death, cardiac death, and stroke. However, the mechanisms of this benefit are unclear.

Objectives. As the second of a 3-part report on this topic, we performed a systematic review of the literature to assess the effect of consumption of omega-3 fatty acids (eicosapentaenoic acid [EPA; 20:5 n-3], docosahexaenoic acid [DHA; 22:6 n-3], and alpha-linolenic acid [ALA, 18:3 n-3])on various CVD risk factors and intermediate markers of CVD in healthy people, people with dyslipidemia, diabetes, or known CVD.

Data Sources. We searched Medline, Embase, Cochrane Central Register of Controlled Trials, Biological Abstracts, and Commonwealth Agricultural Bureau databases for potentially relevant studies.

Study Selection. We screened over 7,464 abstracts and retrieved 807 full text articles. We analyzed 123 studies that met inclusion criteria to address the key questions in this report. We included studies in which the amount of fish or omega-3 fatty acid intake was quantified, less than 6 g of omega-3 fatty acid per day was consumed, and of at least 4 weeks' duration.

Data Extraction. From each eligible study, we extracted information about the study design, population demographics, the amount of omega-3 fatty acids (in supplements or diet) or fish consumed, and outcomes. For RCTs, we extracted information about the randomization, allocation, and blinding techniques to assess methodological quality.

Data Synthesis. We examined the effect of omega-3 fatty acids on potential CVD risk factors – including lipoproteins, apolipoproteins, blood pressure, hemoglobin (Hgb) A_{1c}, C-reactive protein (CRP), hemostatic factors, platelet aggregation, and markers of diabetes – and intermediate markers of CVD – including coronary artery restenosis, carotid intima-media thickness (IMT), exercise tolerance testing, and heart rate variability. We also assessed correlations between long-chain omega-3 fatty acids intake and tissue phospholipid levels.

Among the outcomes we analyzed, omega-3 fatty acids demonstrated a consistently large, significant effect on triglycerides. The trials of triglycerides reported a net decrease in triglycerides of about 10% to 33%. The effect was dose dependent, generally consistent in different populations, and was generally larger in studies with higher mean baseline triglyceride levels. In contrast to studies of fish oils, the single study of a plant oil (ALA) found a net increase in triglycerides. The effect of omega-3 fatty acids on other serum lipids was weaker (up to a 6% increase in HDL).

Outcomes for which a small beneficial effect was found with fish oil supplementation include blood pressure (about 2 mm Hg reduction), restenosis rates after coronary angioplasty (14% reduction), exercise tolerance testing, and heart rate variability. For other evaluated outcomes, including measures of glucose tolerance, the effects of omega-3 fatty acids were either small or inconsistent across studies.

Across studies, we found a direct relationships between dose of consumed omega-3 fatty acids and changes in measured levels of EPA+DHA, either as plasma or serum phospholipids, platelet phospholipids, or erythrocyte membrane phospholipids. The correlation between dose and change in level appears to be fairly uniform, where 1 g supplementation of EPA and/or DHA corresponds to approximately a 1% increase in EPA+DHA level.

Conclusions. A large, consistent beneficial effect of omega-3 fatty acids was found only for triglyceride levels. Little or no effect of omega-3 fatty acids was found for a variety of other cardiovascular risk factors and markers of cardiovascular disease. The benefits of omega-3 fatty acids on reducing cardiovascular disease are not well explained by the fatty acids' effects on the cardiovascular risk factors we examined. A strong, linear association was found across studies between omega-3 fatty acid intake and tissue levels.

Heterogeneity of treatment effect was common among studies across the outcomes evaluated. Given the large amount of heterogeneity across studies, many questions remain about the effect of omega-3 fatty acids in improving potential CVD risk factors and intermediate markers of CVD. Few studies addressed questions related to effect modifiers and only limited conclusions could be made regarding these factors. The optimal quantity and type of omega-3 fatty acid, ratio of dietary omega-6 to omega-3, and duration of treatment remain undefined. Future research is needed to address these issues.

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